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Comparative assessment of nonlinear metrics to quantify organization-related events in surface electrocardiograms of atrial fibrillation

M. Julián [a,*], R. Alcaraz [b], J.J. Rieta [a]

[a] Biomedical Synergy, Electronic Engineering Department, Universidad Politécnica de Valencia, Edificio 7F, 5ª. Camino de Vera s/n. 46022, Valencia, Spain
[b] Innovation in Bioengineering Research Group, University of Castilla-La Mancha, Cuenca, Spain

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Atrial fibrillation (AF) is today the most common sustained arrhythmia, its treatment being not completely satisfactory. Electrical activity organization analysis within the atria could play a key role in the improvement of current AF therapies. The application of a nonlinear regularity index, such as sample entropy (SampEn), to the atrial activity (AA) fundamental waveform has proven to be a successful noninvasive AF organization estimator. However, the use of alternative nonlinear metrics within this context is a pending issue. The present work analyzes the ability of several nonlinear indices to assess regularity of patterns and, thus, organization, in the AA signal and its fundamental waveform, defined as the main atrial wave (MAW). Precisely, Fuzzy Entropy, Spectral Entropy, Lempel–Ziv Complexity and Hurst Exponents were studied, achieving more robust and accurate AF organization estimates than SampEn. Results also provided better AF organization estimates from the MAW than from the AA signal for all the tested nonlinear metrics, which agrees with previous works only focused on SampEn. Furthermore, some of these indices reported a discriminant ability close to 95% in the classification of AF organization-dependent events, thus outperforming the diagnostic accuracy of SampEn and other widely used noninvasive estimators, such as the dominant atrial frequency (DAF). As a conclusion, these nonlinear metrics could be considered as promising estimators of noninvasive AF organization and could be helpful in making appropriate decisions on the patients' management.

1. Introduction

Atrial fibrillation (AF) is the most frequently diagnosed supraventricular arrhythmia in clinical practice [1]. It is associated with decreased survival and quality of life in older adults as well as increased health care costs [2]. However, the mechanisms provoking the onset and termination of this arrhythmia still are not fully understood [2]. Nevertheless, a widely accepted theory, the multiple wavelet hypothesis, associates AF to multiple wavefronts wandering randomly throughout the atria [3,4]. A variety of electrophysiological characteristics, such as the atrial refractory period, mass and conduction velocity can alter substantially the number of simultaneous propagating waves [2]. Thus, the higher the number of circulating wavelets simultaneously propagating in the atria, the lower the likelihood of paroxysmal (i.e. spontaneous self-terminating) AF termination [3]. Similarly, the probability of AF perpetuation in a self-sustained arrhythmia increases with the number of simultaneously circulating wavefronts.

Although AF mechanisms are far from being entirely understood, it is clear that self-sustained complex spatio-temporal patterns of excitation provoke a hierarchical disorganization in the atrial activation [4–6]. AF organization estimates can hence be obtained by quantifying the repetitiveness degree of the atrial activity (AA) signal pattern, thus providing a qualitative idea about the number of simultaneous wavelets wandering throughout the atria. To this respect, several previous works have quantified the regularity in the morphology of fibrillatory (*f*) waves from invasive recordings [7]. Because of abnormal atrial activation patterns during AF such as slow conduction, wave collision and conduction blocks are reflected by very different morphologies of the *f* waves [8], this kind of AF organization analysis can play an interesting role in the understanding of the mechanisms governing its induction and maintenance. In this way, useful information could be reached to improve the non-totally satisfactory current AF knowledge and treatment as well as contributing to make better tailored decisions on the patients' management.

From a clinical point of view, a noninvasive AF organization estimation is very interesting given that the electrocardiogram (ECG) can be acquired in an easy and cheap fashion. Moreover, this

* Corresponding author. Tel.: +34 699 615 892.
E-mail address: majuse@upv.es (M. Julián).

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recording can avoid the typical risks associated to invasive recordings [9]. A widely accepted qualitative AF organization estimator from the ECG is the dominant atrial frequency (DAF) [10]. It is defined as the highest amplitude frequency within the 3–9 Hz band of the AA spectral content [11], its inverse being directly related to atrial refractoriness [12] and, hence, to atrial cycle length [11]. Indeed, previous works have shown that patients with low fibrillatory frequency are associated to longer wavelengths and therefore a lower number of waves circulating simultaneously in the atria. In contrast, patients with shorter wavelengths and higher number of simultaneous wavefronts have reported higher DAF values [13]. On the other hand, a second extended alternative to get a non-invasive estimate of AF organization has been based on a nonlinear regularity index, such as sample entropy (SampEn) [14]. This algorithm quantifies the regularity appreciated in the morphology of the *f* waves from the AA signal fundamental waveform, which has been named in previous works as the main atrial wave (MAW), thus quantifying accurately AA organization [15].

Considering this latter finding together with the fact that nonlinear metrics can provide "hidden information" related to underlying mechanisms in the assessment of physiological time series [16], a variety of nonlinear indices are considered to study AF organization in the present work. Therefore, the aim of the study is to analyze the usefulness of time and spectral series regularity, complexity and statistical self-similarity provided by nonlinear estimators in order to compare the discriminatory ability of the proposed measures in AF organization-dependent events. As a result, pattern repetitiveness in the AA signal and its MAW would be assessed to yield a more robust and accurate noninvasive AF organization estimation. Moreover, the possible complementary information provided by these metrics in the classification of AF organization-dependent events will also be evaluated through a logistic regression analysis.

The remainder of the paper is structured as follows. Section 2 describes the analyzed database, the preprocessing applied to ECG recordings, the nonlinear indices used to estimate AF organization and how their performance is evaluated. Section 3 summarizes the obtained results, which will be next discussed in Section 4. Finally, Section 5 presents the concluding remarks that will lead the manuscript to its end.

2. Methods

2.1. Database

The database analyzed was proposed for the Computers in Cardiology Challenge 2004 and is freely available at PhysioNet [17]. It consists of 80 two-lead (II and V1), 1 min-length ECG signals extracted from Holter recordings of 60 different paroxysmal AF patients. The signals were acquired with a sampling rate of 128 Hz, 16 bits/sample and 5 μV resolution. In addition, they were divided into three groups following their different termination properties. Thus, the database includes 26 non-terminating AF episodes (group N), which continued at least 1 h in AF after the end of the recording, 20 soon-terminating episodes (group S), which terminated 1 min after the end of the recording and 34 immediately terminating episodes (group T), whose termination happened 1 s after the end of the recording. A more detailed description of the database can be found in [18].

2.2. Signal preprocessing

Nonlinear indices were computed from surface lead V1 because the atrial component presents the highest amplitude with respect to the ventricular counterpart in this lead [9]. Additionally, previous works have suggested that the atrial fibrillatory activity is mainly reflected on lead V1 [14,11]. With the aim of improving later analysis, the recordings were forward/backward high-pass (0.5 Hz cut-off frequency) and low-pass (70 Hz cut-off frequency) filtered. In this way, baseline wander and high frequency noise were notably minimized, respectively. Moreover, to remove power line interference, an adaptive band-stop filtering matched at 50 Hz was also applied to the signals [19].

On the other hand, for an appropriate AA study the cancellation of the ventricular activity from the ECG is a mandatory first step. This operation was accomplished by an adaptive QRST cancellation method, which relies on the fact that the atrial and ventricular activities are statistically uncoupled during AF [20]. Briefly, each beat was canceled by subtracting the highest variance eigenvector of its most similar QRST complexes. Before this step, the original ECG signal was upsampled to 1 kHz, using a cubic spline interpolation method. Upsampling improves the time alignment accuracy needed for optimal fit between each single beat and the cancellation template [10].

2.3. Estimation of AF organization through nonlinear metrics

While the aforementioned preprocessing was performed over the whole recording from each patient, the nonlinear indices that will be next described were computed over non-overlapped 10 s-length segments. After analyzing these AA segments, their average result was considered as an AF organization estimation. The particular segment length of 10 s was chosen as a tradeoff between robustness, time resolution and computational cost. Moreover, ambulatory ECG recordings are usually about 10 s in length. Therefore, the use of this computational data length seems appropriate with regard to possible future clinical applications of the studied indices.

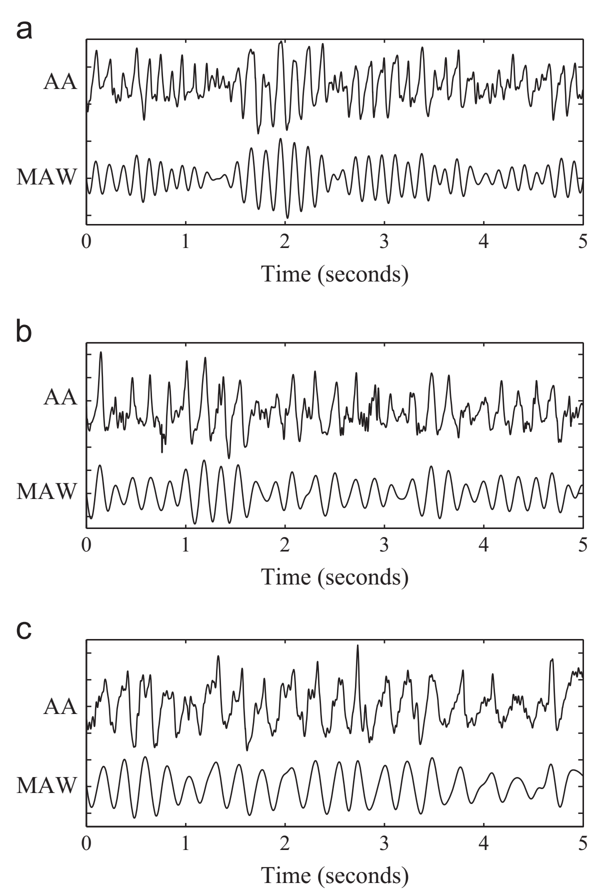

Fig. 1. Examples of AA and MAW waveforms for a typical (a) non-terminating AF episode, (b) soon-terminating AF episode and (c) immediately terminating AF episode.